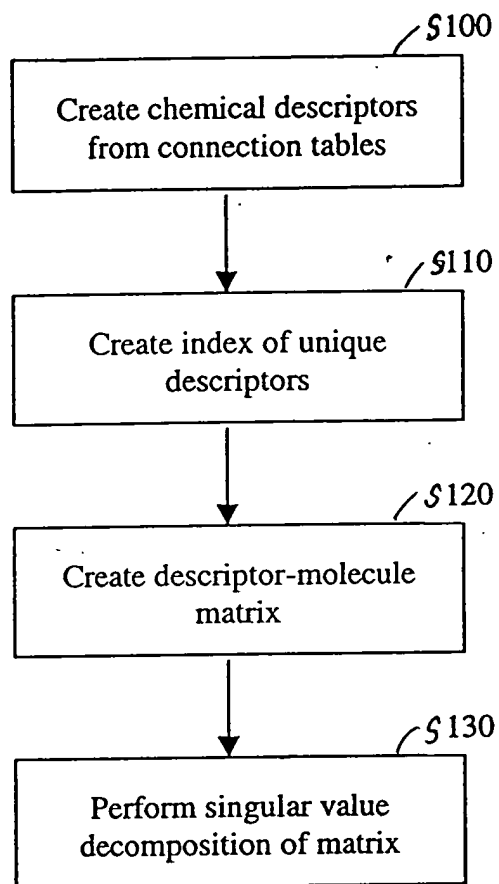


Figure 1. Process Flow Chart

LaSSI Database Construction



Query Handling

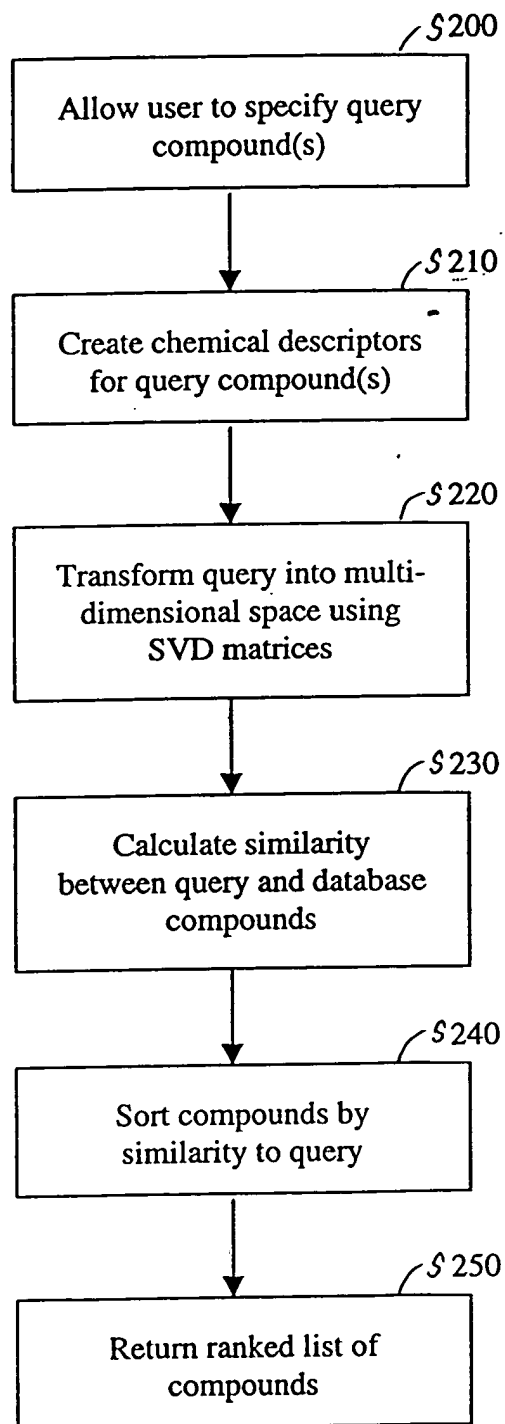
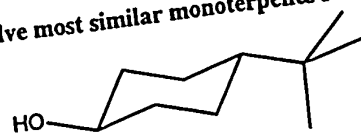


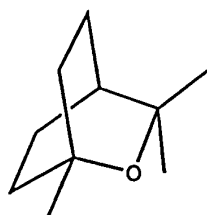
Figure 2. Probe and its twelve most similar monoterpenes selected using 2 singular values



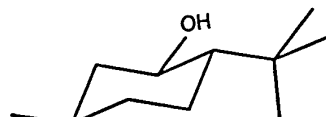
4-*t*-butylcyclohexanol
Probe molecule



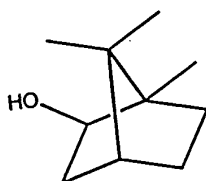
terpin
0.531



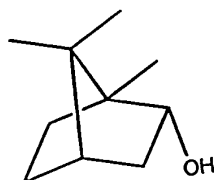
eucalyptol
0.435



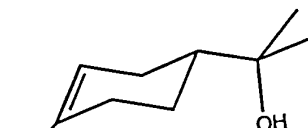
menthol
0.389



isoborneol
0.389

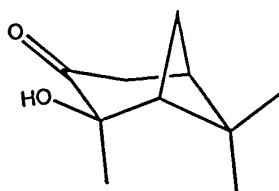


borneol
0.389

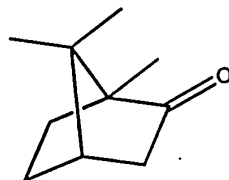


α -terpinol
0.361

6 Most similar by Tanimoto similarity



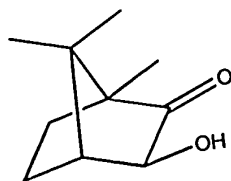
oxipinocamphone
1.0000



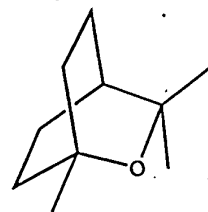
camphor
0.9998



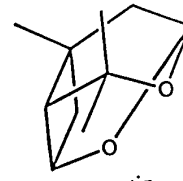
terpin
0.9997



3-hydroxycamphor
0.9997



eucalyptol
0.9995



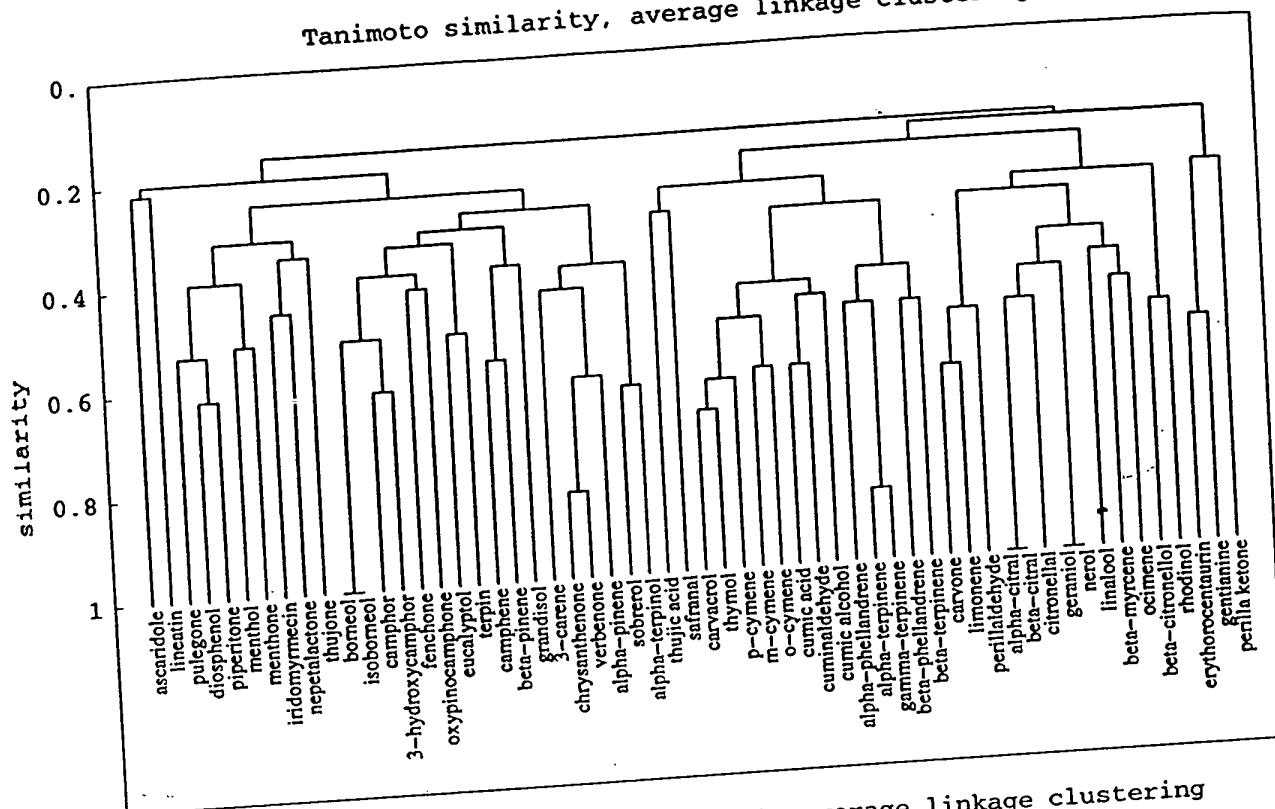
lineatin
0.9992

6 Most similar by LaSSI similarity

00040:00040

Figure 3. Dendrograms Showing Similarities For Tanimoto and LaSSI

Tanimoto similarity, average linkage clustering



LaSSI similarity (2 singular values), average linkage clustering

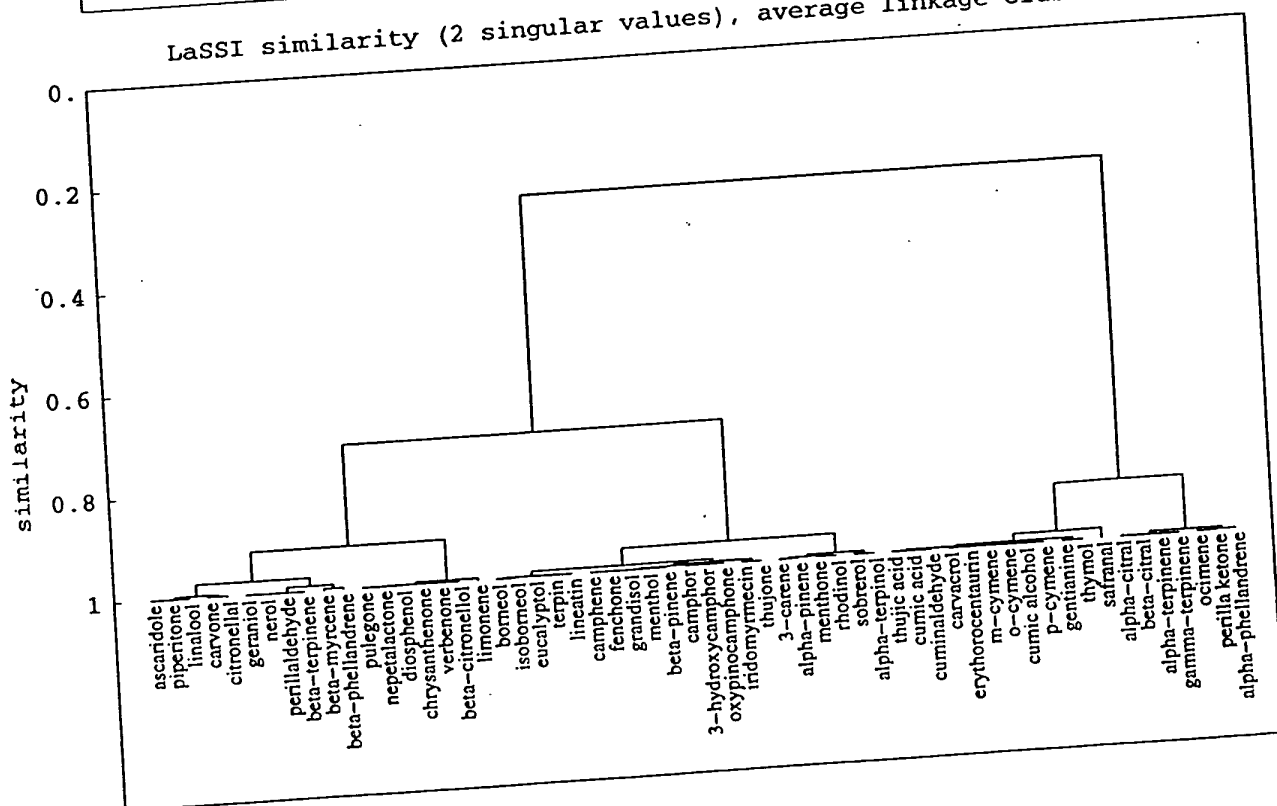
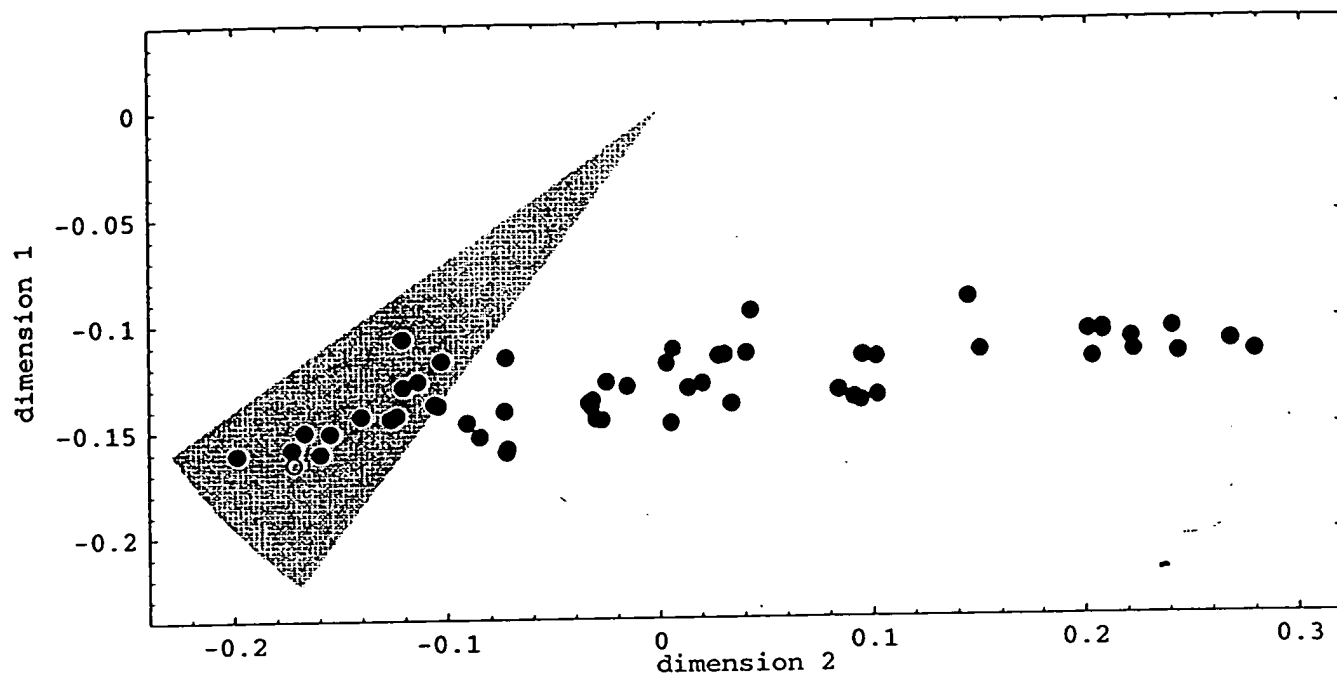


Figure 4. Two-dimensional Plot of Example Database Compounds and Probe Compound



000140-66634560

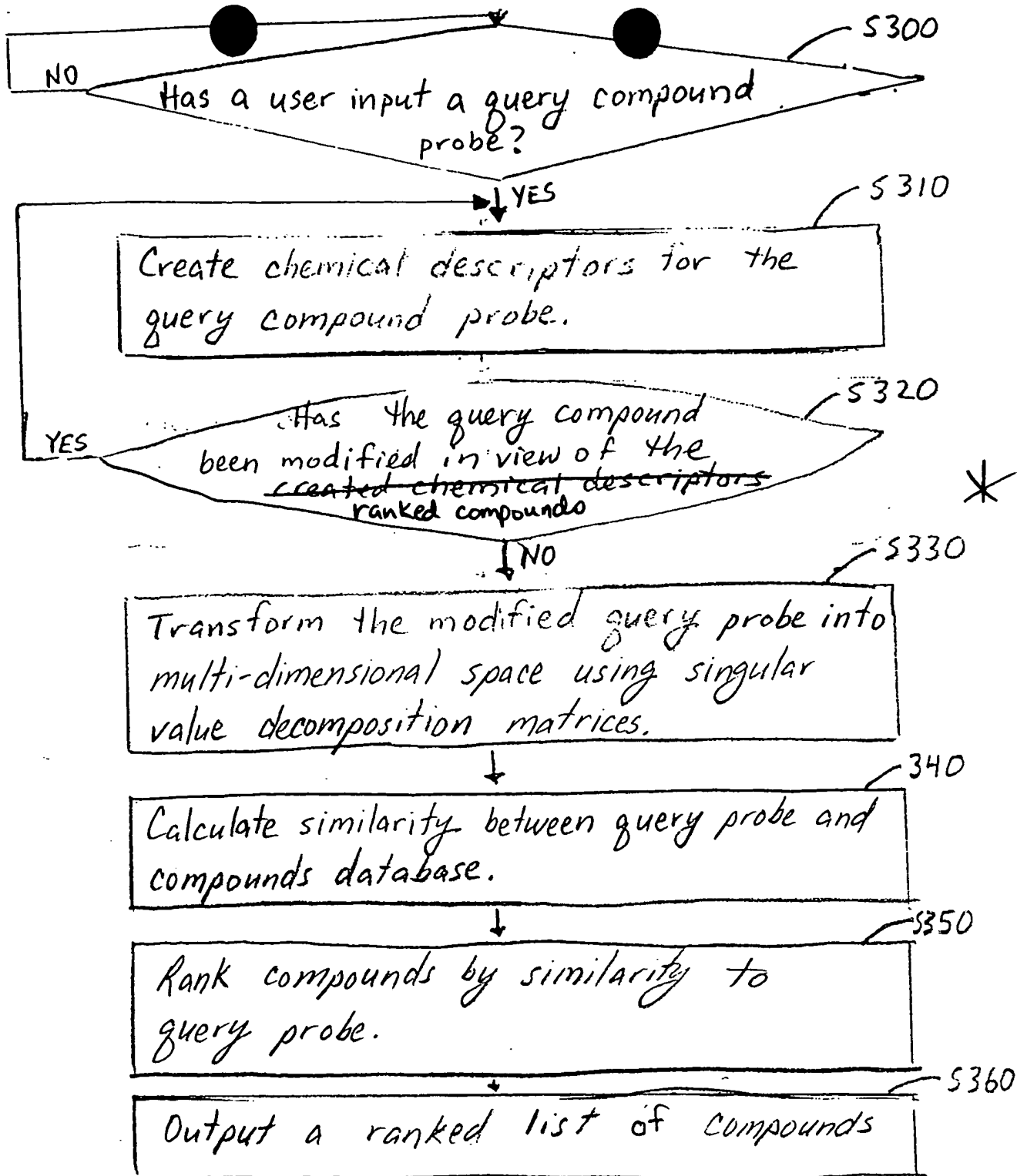
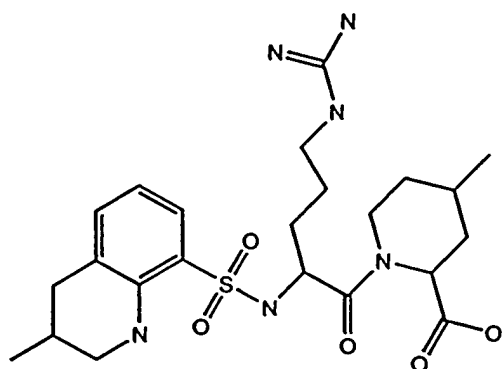


Figure 5

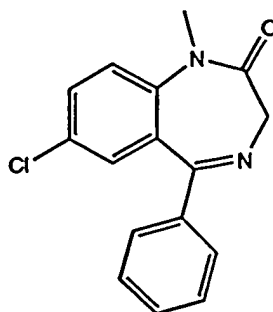
SURESH,
S320 is really not
right. We need to
talk about this
more. Richard

Figure 6a.

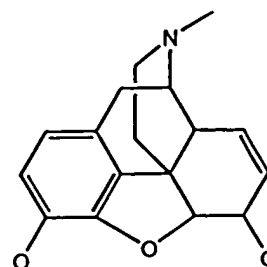
Standard probes used in this study. Each is labeled by the MDDR external registry, its name, and associated activity.



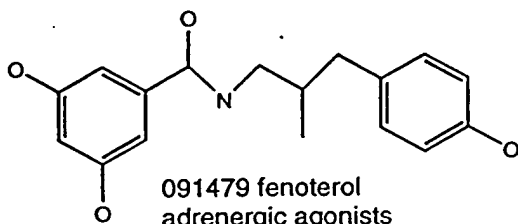
090744 argatroban
thrombin inhibitors



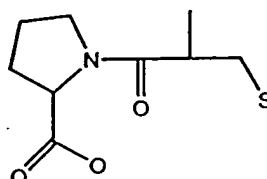
091323 diazepam
anxiolytics



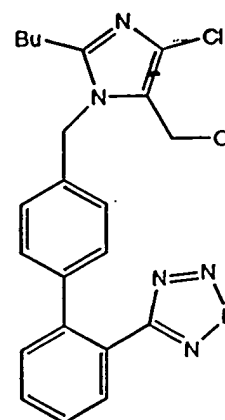
091342 morphine
opioid analgesics



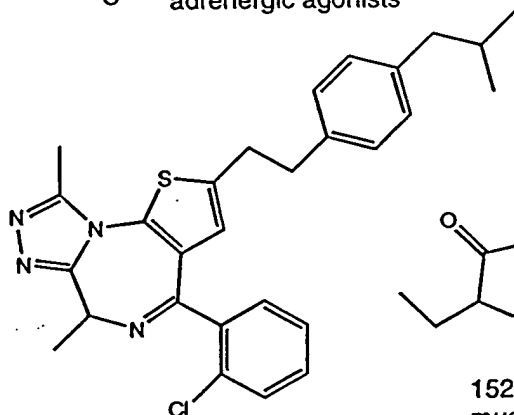
091479 fenoterol
adrenergic agonists



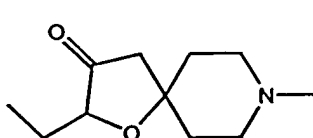
115230 captopril
ACE inhibitors



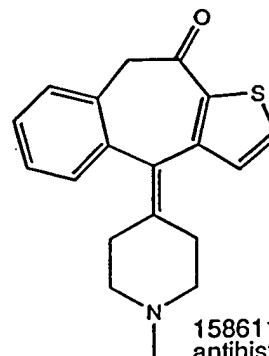
140603 losartan
All blockers



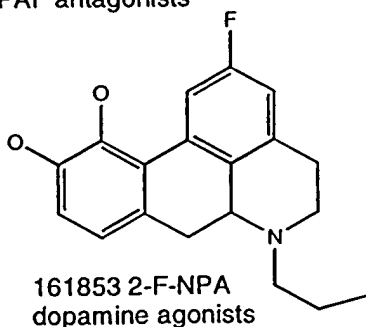
144822 israpafant
PAF antagonists



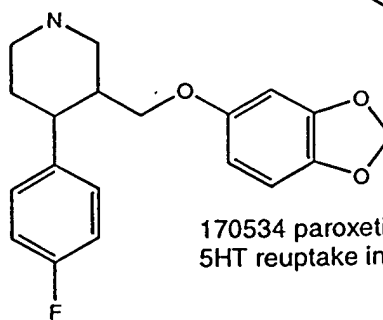
152580 YM-954
muscarinic agonists



158611 ketotifen
antihistamines



161853 2-F-NPA
dopamine agonists



170534 paroxetine
5HT reuptake inhibitors

000110-66694560

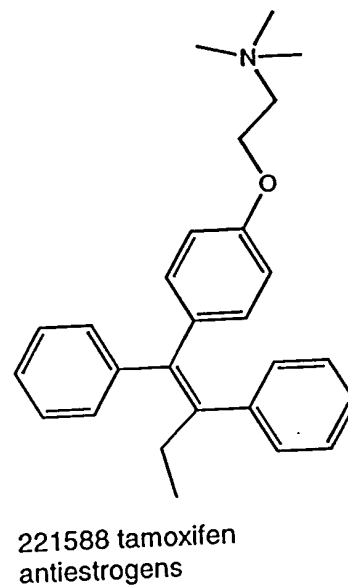
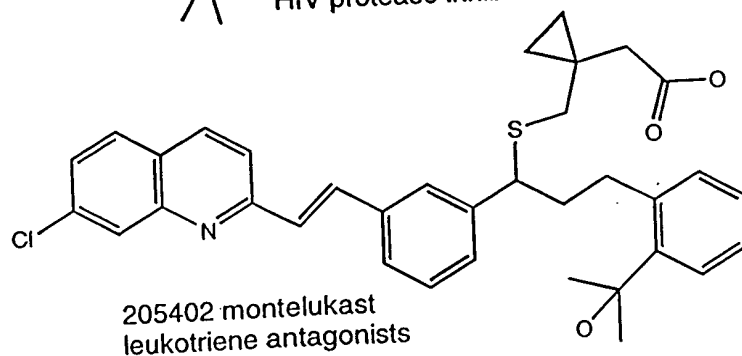
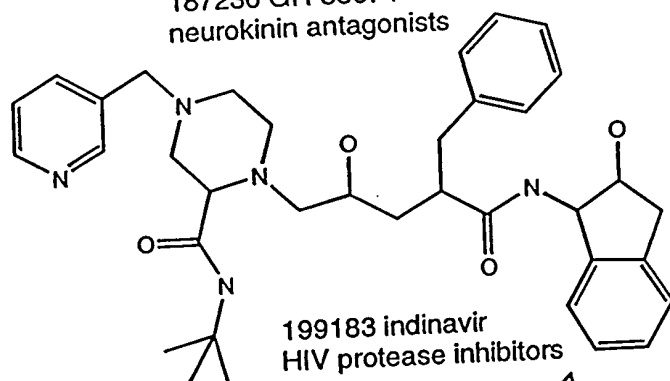
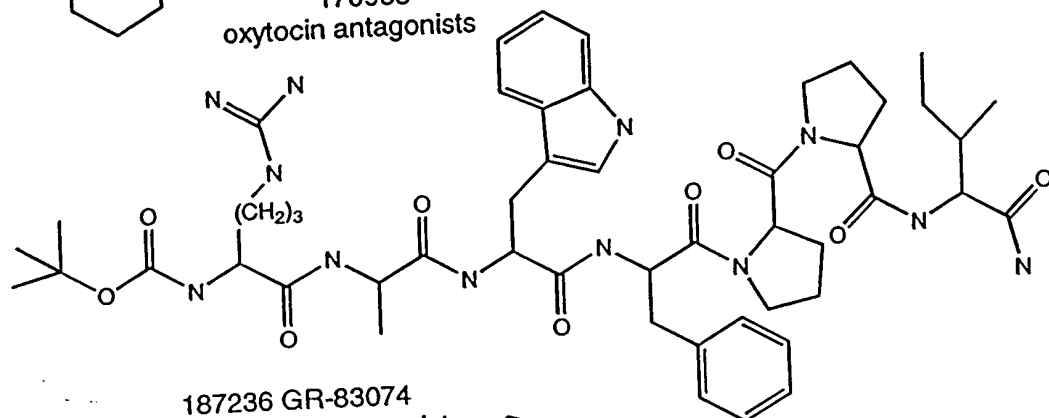
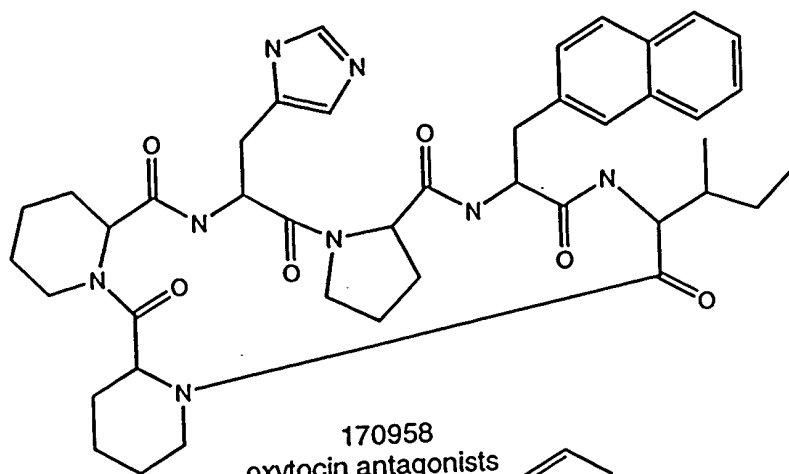
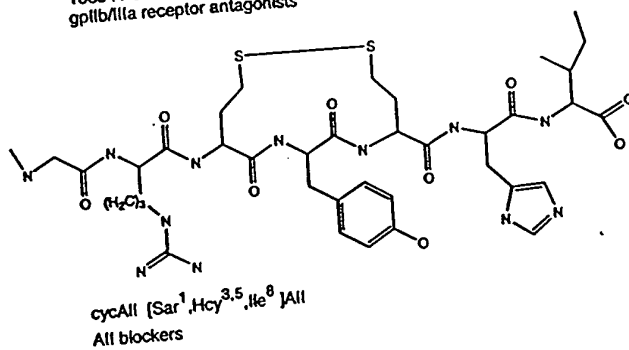
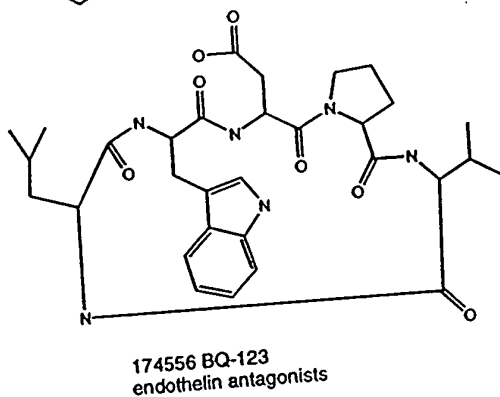
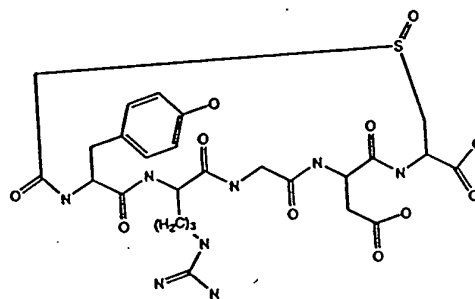
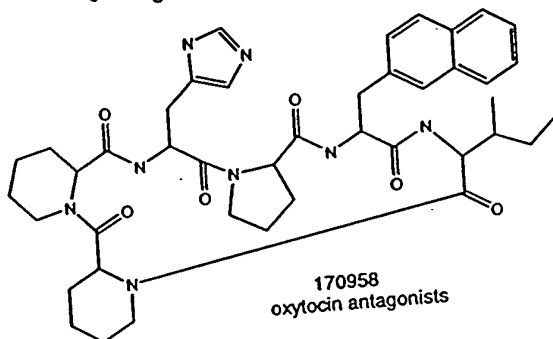
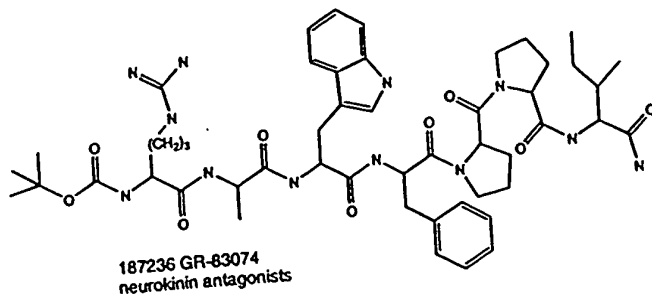
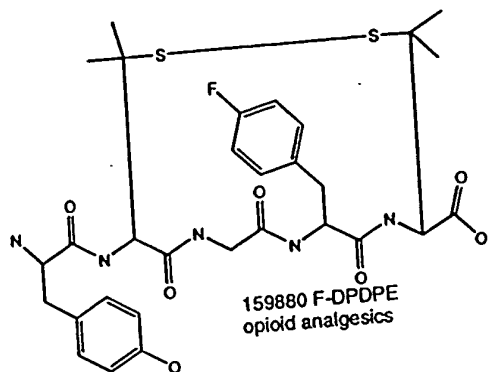


Figure 6b

Figure 7

Probes used for peptide -> non-peptide tests.



000140-66634560

Figure 8. The initial enhancement for LaSSI APTT vs the number of singular values shown for three examples.

Initial Enhancement vs Singular Values

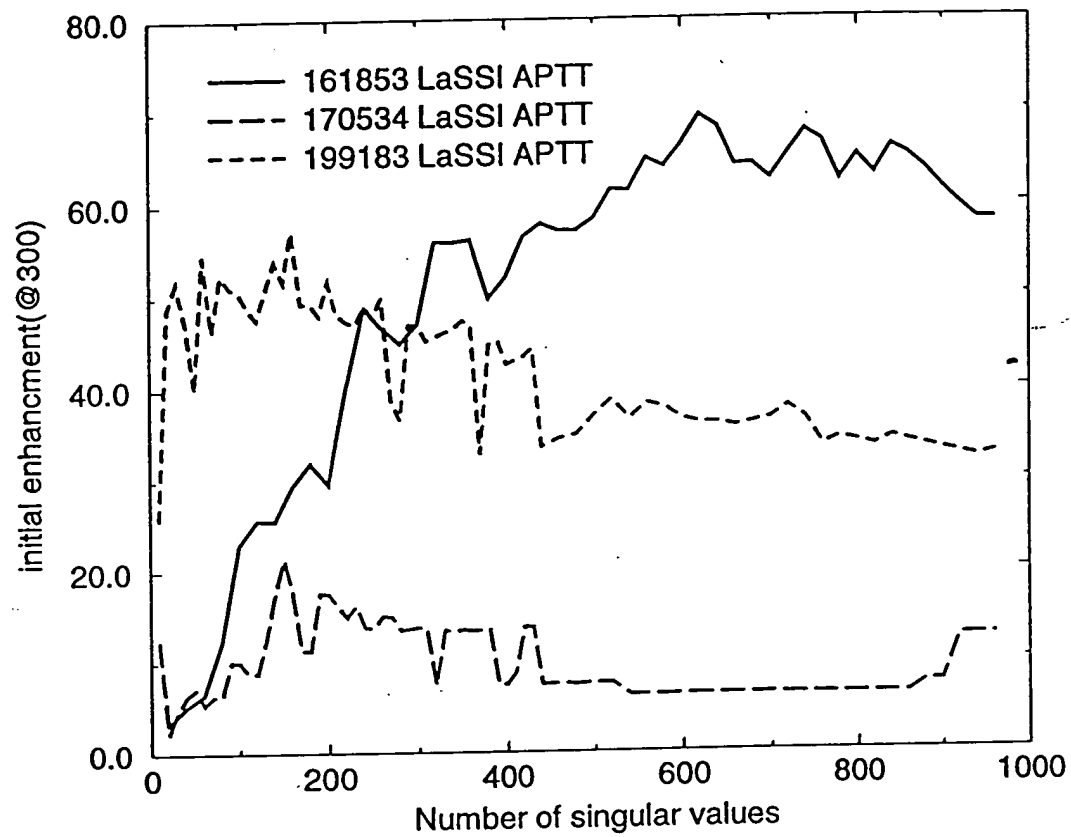
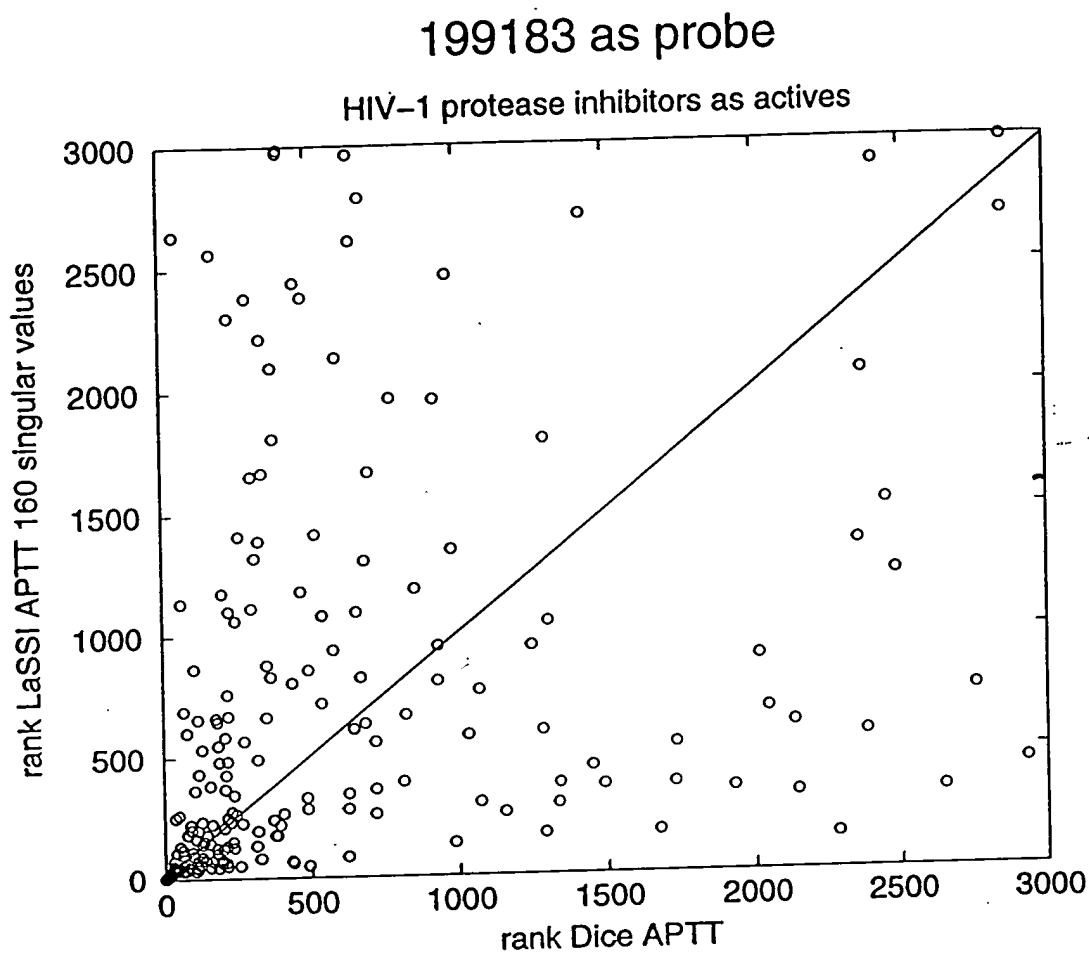


Figure 9. The correlation of rank for Dice APTT and LaSSI APTT. The example is 199183 using 170 singular values. Each circle represents a HIV protease inhibitor.



000740-66E94560

10
Figure 9. Selected compounds that have extremely different ranks in Dice APTT vs LaSSI APTT. The examples are 161853 with 800 singular values, 170534 with 150 singular values. The ranks in tw types of search are indicated.

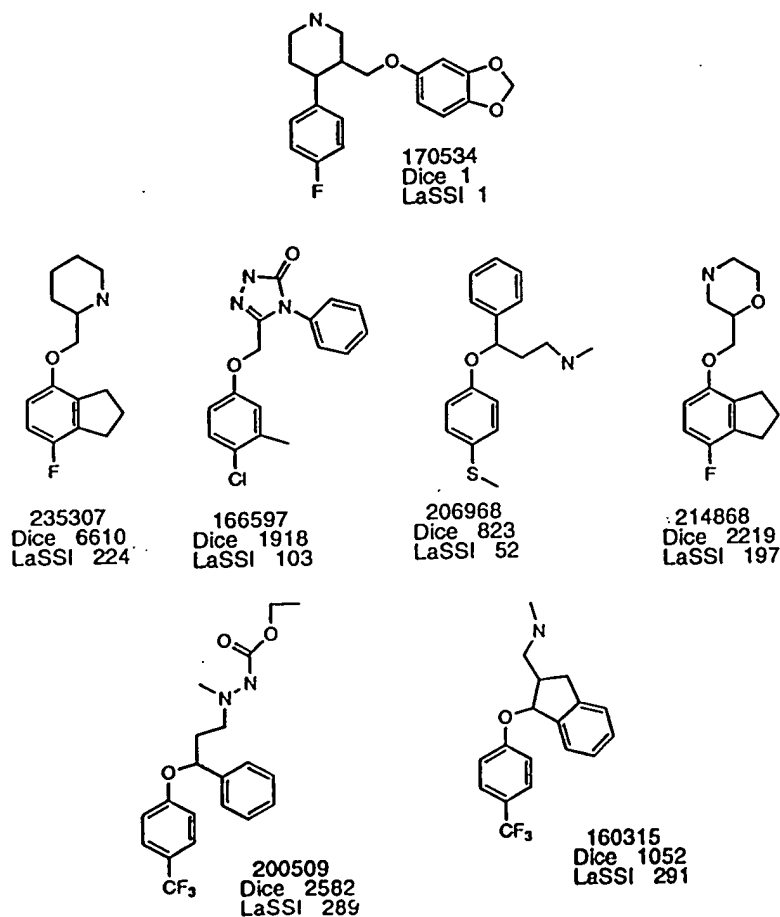
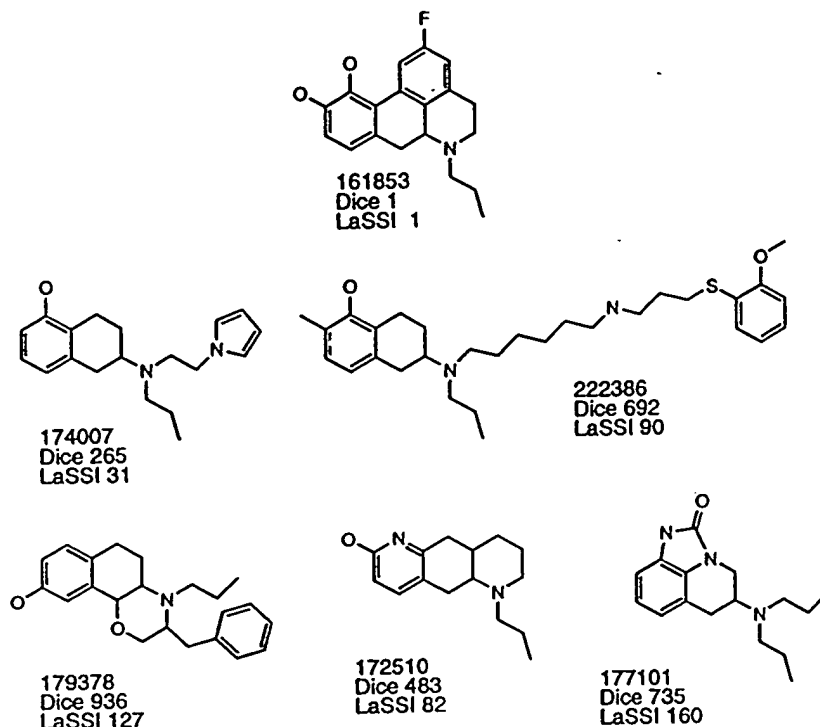




Figure 11

Mean similarity of the probe to each molecule in the top scoring 300 compounds (MSP300) for three random sets of 300 compounds from MDDR would be 0.12-0.14.

MSP300

Dice TT

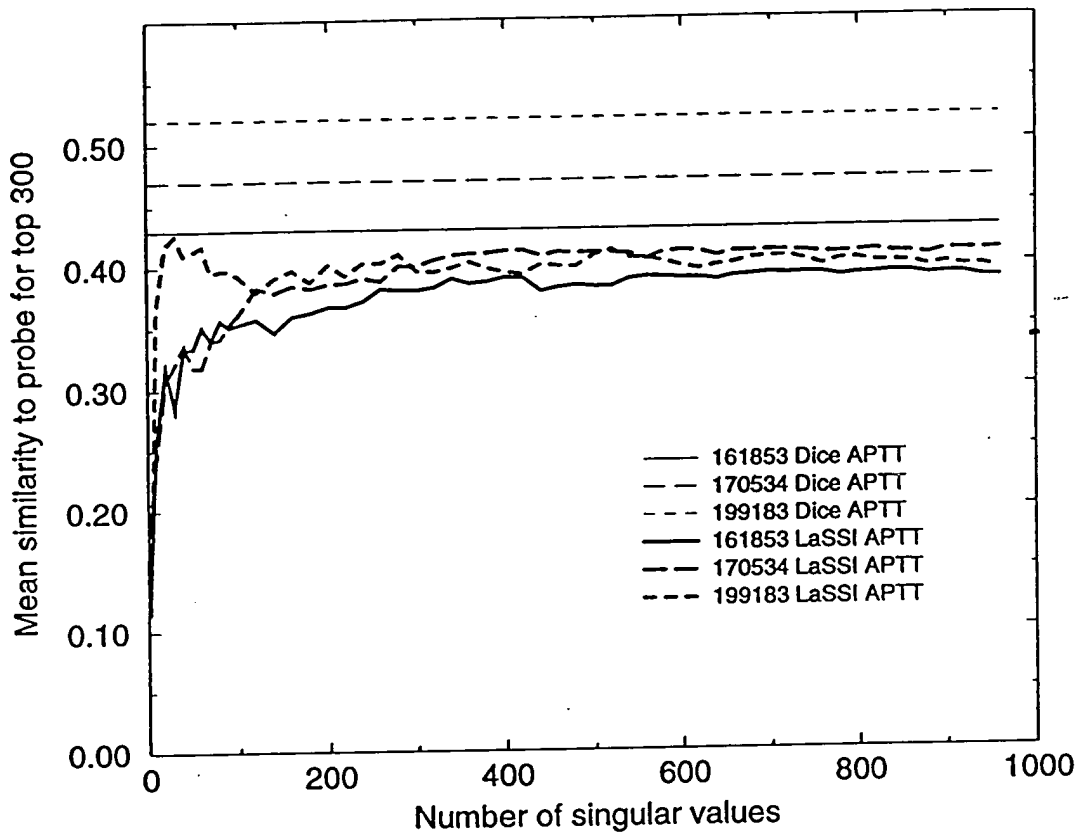


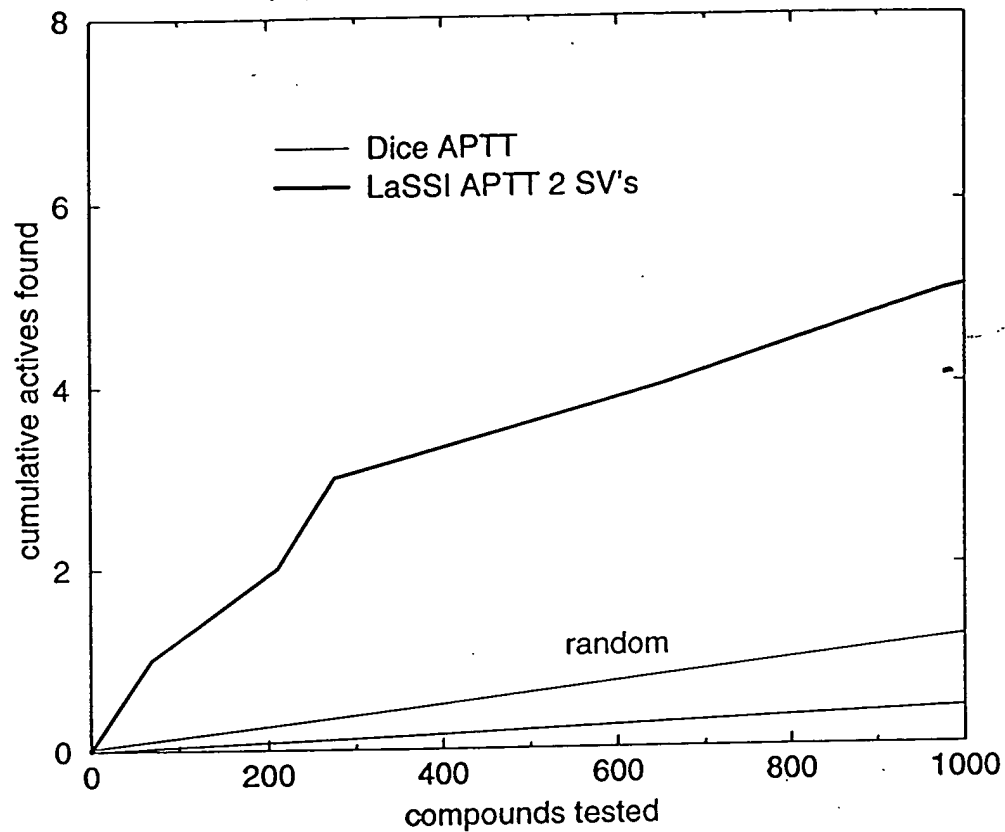


Figure 12

Cumulative actives found vs compounds tested for 187236 as a probe. The actives are oxytocin antagonists that do not contain a dipeptide moiety.

187236 as probe

nonpeptide neurokinin antagonists as actives



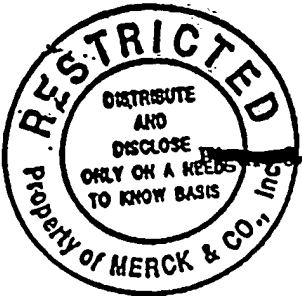
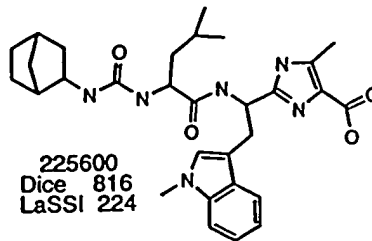
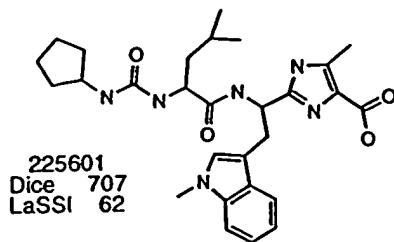


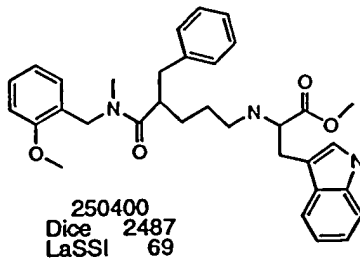
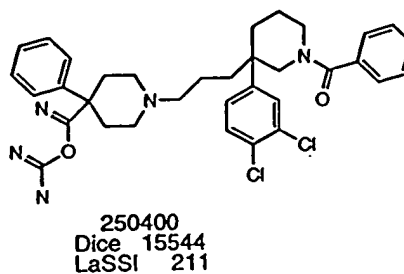
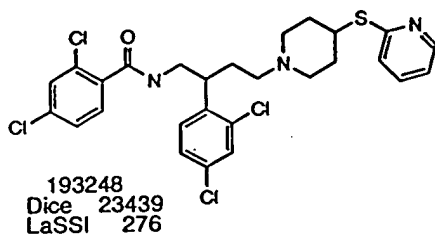
Figure 13

Selected non-peptide compounds that have extremely different ranks in Dice APTT vs LaSSI APTT for the statistically significant peptide & non-peptide examples.

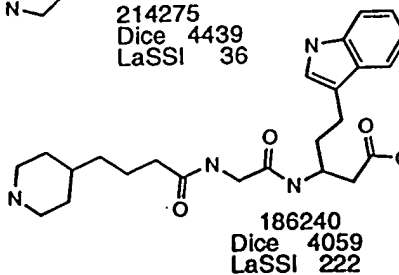
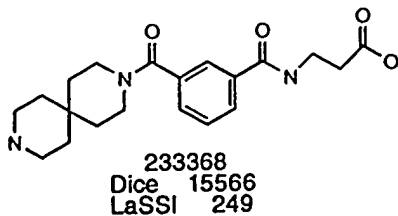
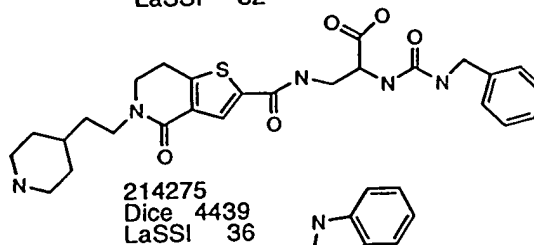
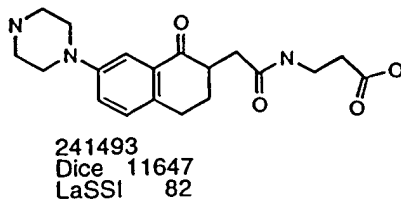
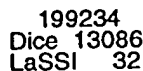
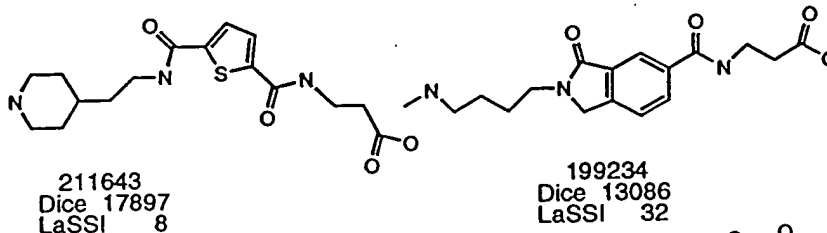
174556 endothelin antagonists (9 SV's)



187236 neurokinin antagonists (2 SV's)



188541 gp11b/11a receptor antagonists (15 SV's)



000140-000000

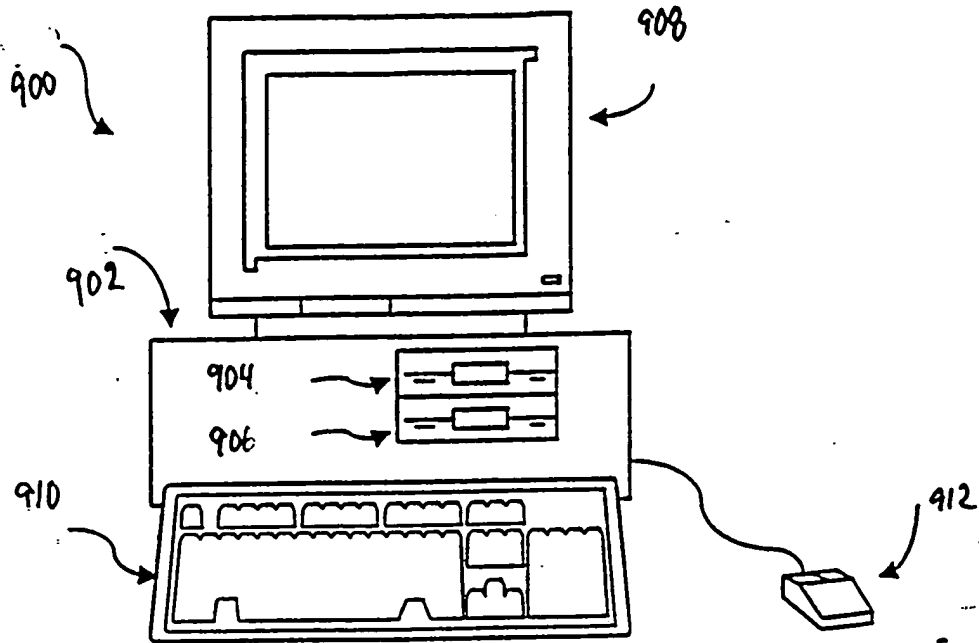


FIG. 14

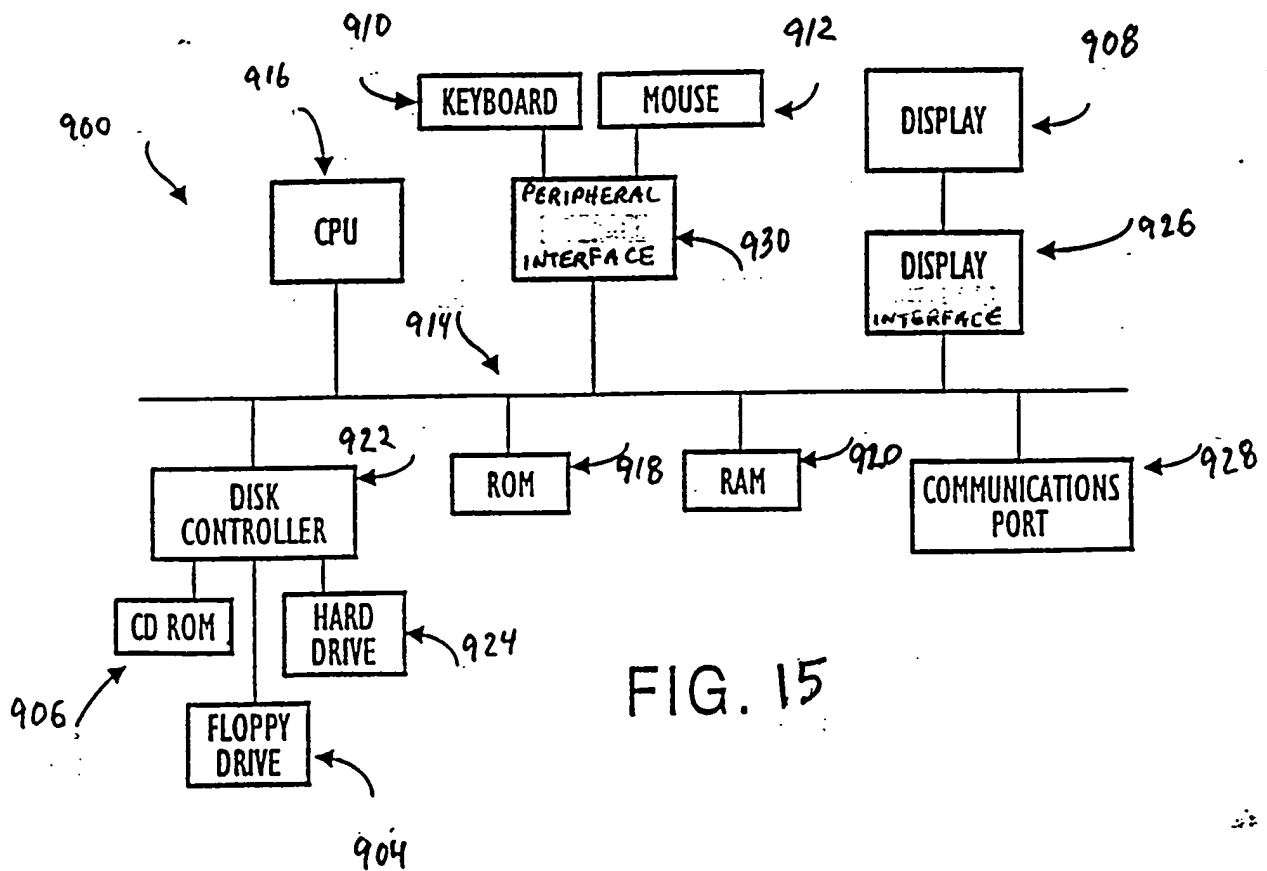


FIG. 15

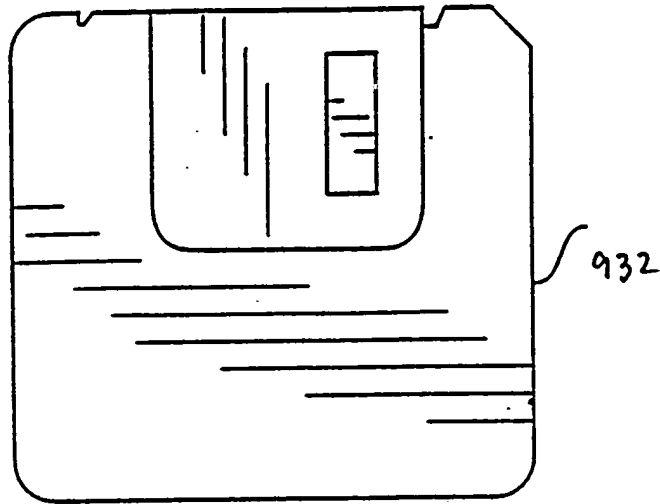


FIG. 16